REMARKS

The Examiner made a determination that the Applicants were not entitled to the benefit of an earlier filing date. The Examiner rejected claims 22-27, 30, 31, and 35-41 under 35 U.S.C. § 112, first paragraph for failing to enable any person skilled in the art to use the invention commensurate in scope with these claims. The Examiner rejected claims 22-41 under 35 U.S.C. § 112, first paragraph for failing to describe the subject matter in the specification in such a way as to enable one skilled in the art to make and/or use the invention. The Examiner also rejected claims 22-27 and 35-41 under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse the rejections, determination of the benefit of the priority date, and request that the Examiner consider the following remarks in response to the Office Action.

Priority Determination:

The Examiner asserts that the subject matter defined in pending claims 22-34 has an effective filing date of December 1, 1999 due to a lack of enablement for the claimed invention in the parent (or provisional) application 09/254,311 (the '311 application), filed March 3, 1999. Applicants respectfully traverse this determination for at least the following reasons. The '311 application discloses the polypeptide, as the Examiner acknowledges and asserts several specific, substantial and credible utilities for the claimed invention. For example, the '311 application discusses the use of the claimed invention in assays including uses as hybridization probes, in chromosome and gene mapping and in the generation of anti-sense RNA and DNA (see p. 36)

Furthermore, Applicants submit that the in addition to support found in the '311 application, the specification of the provisional application 60/075,945, filed on February 25, 1998, to which the '311 application claims priority also asserts several specific, substantial and credible utilities for the claimed invention. For example, the '945

application discusses the use of the claimed invention in various applications in the art of molecular biology, including uses as hybridization probes, in chromosome and gene mapping and in the generation of anti-sense RNA and DNA. (see p. 21)

For at least these reasons, Applicants respectfully submit that the proper priority date for the claimed invention is at least March 3, 1999. The Applicants request that the Examiner reconsider the determination of the benefit of the earlier filing date.

Rejection under 35 USC § 112, first paragraph:

Enablement

The Examiner has rejected claims 22-41 under 35 USC § 112, first paragraph, for allegedly not being enabled by the specification. Applicants respectfully submit that the claims are enabled by the specification and request reconsideration by the Examiner.

In the rejection of claims 22-27, 30, 31, and 35-41, the Examiner noted that while the claims are enabled for an isolated nucleic acid encoding a polypeptide having at least 80% sequence identity to the polypeptide of SEQ ID NO: 83, or to the polypeptide lacking the signal peptide which polypeptide inhibits proliferation of stimulated T-lymphocytes, the specification does not provide enablement for fragments or variants that are not required to have such activity.

The Applicants have herein amended claims 22-26 to include a functional limitation. Specifically, Applicants have amended each of these claims to indicate that the polypeptide encoded by the nucleic acid is able to inhibit the proliferation of stimulated T-lymphocytes. This function of the claimed nucleic acids is described throughout the specification, and is specifically supported by Example 34 on page 141.

Claims 27-35 have not been amended. Claim 27 is directed to the wild-type nucleic acid disclosed in the specification in Figure 31 (SEQ ID NO:82) and Figure 32 (SEQ ID NO: 83) and thus is enabled by the specification. Applicants have deposited Clone DNA45410-1250 with the American Type Culture Collection (ATCC). The deposit of

Clone DNA45410 satisfies the enablement requirement of 35 U.S.C. §112, first paragraph. *In re Argoudelis*, 434 F.2d 1390, 1392 (CCPA 1970). Claims 28-34 depend from independent claim 27 and are also enabled by the disclosure for the same reasons discussed above. Accordingly, the Applicants assert that these rejections are improper and respectfully request that these rejections be withdrawn.

Independent claim 35 is directed to an isolated nucleic acid that hybridizes to the wild-type nucleic acid disclosed in the specification in Figure 31 (SEQ ID NO:82), Figure 32 (SEQ ID NO: 83) or the cDNA deposited under ATCC accession number 209621 and thus is eanbled by the specification for the reasons discussed for independent claim 27. Claims 36 and 37 depend from independent claim 35 and are also enabled for the reasons discussed above.

Claim 38 includes the functional limitation in amended claim 22. The functional limitation indicates that the polypeptide encoded by the nucleic acid of claim 22 is able to inhibit the proliferation of T-lymphocytes. Claims 39-41 depend from claim 38 and thus, include the functional limitation. Furthermore, Applicants have submitted the Claims 33 and 34, due to their dependency on newly amended independent claim 22, now include the functional limitation added by this amendment.

The Examiner further rejected claims 22-41 35 USC § 112, first paragraph, for allegedly not being enabled by the specification to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Applicants respectfully assert that the claimed invention is enabled by the specification commensurate in scope of the claims. The specification teaches one of skill in the art how to use the claimed nucleic acids encoding PRO361 polypeptides and does not require undue experimentation. As discussed below, the specification enables use of the claimed nucleic acid sequences as probes for

detecting full length cDNAs and variants thereof. Enablement of a single utility is sufficient. *In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991).

In *In re Wands*, 858 F. 2d 731, 737 (Fed. Cir. 1988), the Federal Circuit stated:

> The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art (citations omitted). The text is not merely quantitative, since *a considerable amount of experimentation is permissible*, if it is merely routine, or *if the specification provides a reasonable amount of guidance* with respect to the direction in which the experimentation should proceed (emphasis added).

The *Wands* court set forth the following factors to analyze in determining whether an application is enabled: (1) the nature of the invention, (2) the state of the prior art, (3) the relative skill of those in the art, (4) the level of predictability in the art, (5) the existence of working examples, (6) the breadth of the claims, (7) the amount of direction or guidance by the inventor, and (8) the quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

As the Examiner indicated, the nature of the invention encompasses an isolated nucleic acid encoding a polypeptide having the sequence of SEQ ID NO: 83 and various structural variants. However, Applicants respectfully traverse the Examiner's limitation of the teaching in the specification to the use of nucleic acids for gene therapy on page 73. Applicants respectfully submit that the specification generally teaches using the claimed nucleic acid sequences in various applications in the art of molecular biology, including uses as hybridization probes, in chromosome and gene mapping and in the generation of anti-sense RNA and DNA (see pages 69 to 71). Additional applications in the art of molecular biology include binding assays, generation of transgenic animals, gene therapy, chromosome identification and tissue typing (see pages 72 to 73).

The specification provides ample description to enable one skilled in the art to make or use the claimed nucleic acid sequences. For example, on page 64, the specification teaches how to isolate the DNA encoding PRO from a cDNA library from human tissue, a genomic library or by known synthetic procedures. The libraries can be screened with antibody or oligonucleotide probes to identify the PRO gene or protein encoded by the PRO gene. A method for the isolation of cDNA clones encoding human PRO361 is described in Example 17 on page 109. The entire nucleotide sequence is shown in Figure 31 (SEQ ID NO: 82). Figure 31 indicates a single open reading frame, a translational initiation site at nucleotide positions 226-228 and a stop codon at nucleotide positions 1519-1521.

One skilled in the art may then use the claimed nucleic acid sequences, for example, as described in the specification on page 70 to isolate full-length PRO cDNA from a cDNA library or to isolate naturally-occurring variants of PRO or PRO from other species having the desired sequence identity to the native PRO sequence (SEQ ID NO: 82). An example taught by the specification on page 70 describes a screening method comprising isolating the coding region of the PRO gene using the known DNA sequence to synthesize a selected probe of about 40 bases. Hybridization probes may be labeled by a variety of labels. One can then use the labeled probe to isolate PRO or variants thereof. One skilled in the art recognizes that degeneracy exists in the genomic code and additionally some species to species or individual to individual variation exists in isolated nucleic acid sequences in non-crucial regions but the substantial function or activity of the polypeptide encoded by the nucleic acid sequence isolated remains the same.

Applicants assert that the specification as discussed above illustrates that the description of the claimed invention was sufficient to enable one skilled in the art to practice the invention commensurate with the scope of the claims. Enablement of a single utility is sufficient. *In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991).

An analysis of the prior art as of the effective filing date of the present application shows successful application of various molecular biology techniques using isolated nucleic acids encoding polypeptides when the sequence is disclosed such as with a deposit in the ATCC. As discussed below, the prior art demonstrates successful use of mucin family genetic markers, a family to which the claimed isolated nucleic acid has homology, for the detection of cancer in various tissues. Applicants respectfully traverse the Examiner's limitation of discussion of the state of the prior art to a discussion of gene therapy. Several of the applications in the art of molecular biology discussed in the specification are readily available and useful techniques to those skilled in the art.

The relative skill of those in the art of the subject matter of the present application is high.

The level of predictability in the art of the subject matter of the present invention is predictable. One skilled in the art can use the claimed nucleic acids in various molecular biology applications without undue experimentation. Applicants respectfully traverse the Examiner's characterization of the invention as unpredictable based solely on the discussion of gene therapy.

Working examples are disclosed in the specification that enable on of skill in the art to make or use the claimed invention. For example, a working example is disclosed on page 109 for the isolation of cDNA clones encoding human PRO361. Additionally, an example of PRO361 inhibitory activity in a mixed lymphocyte reaction assay is disclosed on page 141. An example of tissue expression distribution for the nucleic acid DNA45410-1250 using specific oligonucleotide probes is disclosed on page 142. Applicants respectfully traverse the Examiner's focus on gene therapy applications.

Additionally, Applicants traverse the Examiner's characterization of the quantity of experimentation necessary to carry out the claimed invention as being high and that the prior art together with the present specification do not enable one

skilled in the art to use the claimed methods. Applicants respectfully submit that the claims are directed to isolated nucleic acids, vectors, and host cells and not to any method. Applicants submit that the specification discloses to one skilled in the art how to make and use the claimed invention without undue experimentation. For example, the specification provides adequate guidance for isolating PRO and variants thereof from cDNA libraries, using a labeled probe to one of skilled in the art to make and use the claimed invention. Applicants acknowledge in the specification on page 70 that screening conditions may be varied depending on the desired clones to be isolated, however variations in the screening conditions clearly cannot be considered undue experimentation.

Applicants respectfully assert that the deposit of Clone DNA45410-1250 with the ATCC, combined with the methods for making and using the claimed invention described in the specification and the methods well known to those of skill in the art enable a skilled artisan to practice the full scope of the claimed invention.

According to the MPEP § 2164.01, "the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation."

Accordingly, the Applicants submit that these rejections are improper and respectfully request that these rejections be withdrawn.

Written Description

The Examiner rejected claims 22-27 and 35-41 under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants submit that claims 22-27 and 35-41 are adequately described in the specification.

The applicants have herein amended claims 22-26 to include a functional limitation. Specifically, Applicants have amended each of these claims to indicate that the isolated polypeptide encoded by the nucleic acid is able to inhibit the proliferation of stimulated T-lymphocytes. This function of the claimed nucleic acids encoding the isolated polypeptides is described throughout the specification, and is specifically supported by Example 34 on page 141. Claims 38-41 now include the functional limitation of amended claim 22.

Claims 27 and 35-37 are directed to wild-type sequences and thus the specification recites distinguishing, identifying characteristics, sufficient to satisfy the written description requirement with respect to claims 27, and 35-37.

Accordingly, all independent claims directed at variants of the wild-type now contain both structural and functional characteristics that identify the claimed polypeptides. Together, the structural and functional characteristics distinguish the isolated polypeptides that belong to the claimed genus from those excluded from the genus. Moreover, both the structural and functional characteristics are fully described in the specification as originally filed. Thus, the claims, as amended, define subject matter that is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed.

Accordingly, and respectfully request that the Examiner reconsider and withdraw the rejection.

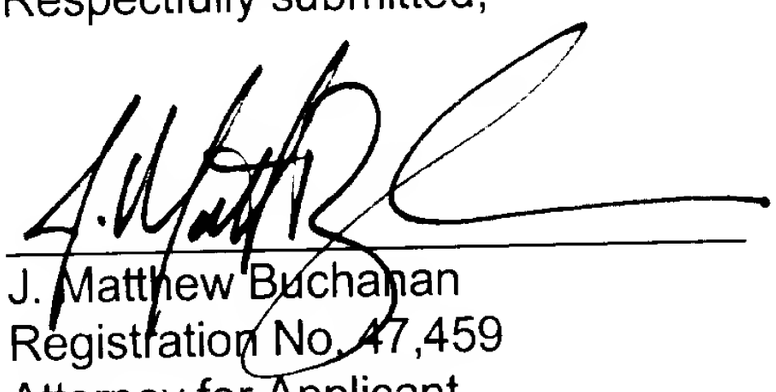
For all these reasons, Applicants assert that the specification recites distinguishing, identifying characteristics, sufficient to satisfy the written description requirement with respect to claims 27 and 35-41. Applicants respectfully assert that the amendments to claims 22-26 fully overcome the rejection of claims directed to variants of the wild-type sequence. Based upon this, Applicants clearly had possession of the invention at the time the application was filed. Applicants respectfully request the Examiner withdraw this ground of rejection.

CONCLUSION

Applicants believe this Amendment and Request for Reconsideration fully responds to the Office Action. Applicants respectfully request the Examiner grant early allowance of this application. The Examiner is invited to contact the undersigned attorney for the Applicant via telephone if such communication would expedite this application.

Applicants believe no fee is due in connection with the filing of this Amendment, however, should any fees be deemed necessary for any reason relating to this paper, the Commissioner is hereby authorized to deduct said fees from Brinks Hofer Gilson & Lione Deposit Account No. 23-1925. A duplicate copy of this document is enclosed.

Respectfully submitted,



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